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Clinical outcomes and risk factors of coronary artery aneurysms after successful percutaneous coronary intervention and drug-eluting stent implantation for chronic total occlusions

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ABSTRACT

Objective: The study aimed to analyze the risk factors and long-term outcomes associated with coronary artery aneurysms (CAAs) after successful percutaneous coronary intervention (PCI) and drug-eluting stent (DES) implantation in patients with CTOs.
Background: There are sporadic data available on post-procedure CAAs after transcatheter revascularization for CTOs.
Methods and results: A total of 141 patients with 149 CTOs who underwent successful CTO-PCI and DES implantation with angiographic follow-up from 2004 to 2010 were included. Patients were divided into CAA group and non-CAA group according to the presence of CAAs in the follow-up angiography. The independent predictors and major adverse cardiac events (MACEs) including cardiac death, myocardial infarction (MI) and target-vessel revascularization (TVR) were compared between two groups. The incidence of CAAs was 11.4% (17/149) after index procedure. Multivariate analysis showed that age (OR: 0.925, CI 0.873–0.980, P = 0.008), ostial occlusion (OR: 6.715, CI 1.473–30.610, P = 0.014), the parallel wire technique (OR: 6.167, CI 1.709–22.259, P = 0.005) and DES length (OR: 1.030, CI 1.002–1.058, P = 0.036) were the independent predictors of CAAs after successful CTO-PCI and DES implantation. MACEs were similar between two groups (adjusted hazard ratio 0.670; 95% CI 0.160–2.808; P = 0.584) during the 5-year follow-up.
Conclusions: The independent predictors of CAAs after successful CTO-PCI and DES implantation are age, ostial occlusion, the parallel wire technique and DES length. CAAs after index procedure are not frequently associated with adverse clinical events under dual antiplatelet therapy. Further large clinical studies are warranted to explore the clinical implications of patients with this distinct new entity.

1. Introduction

Approximate one third of the patients with significant coronary artery disease on angiography have at least one chronic total occlusion (CTO) [1,2]. Over the last decade, remarkable progress has been achieved in the percutaneous management of coronary artery disease. However, recanalization for CTOs of native coronary arteries is still regarded as the "last frontier" of percutaneous coronary intervention (PCI) due to its high rates of procedural complications and failure [3].

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In the 1990s, the procedural success rates of CTO-PCI were only 48%–76% [4–6]. With improved operator experience, dedicated devices and procedural techniques, the success rates have steadily increased in the past few years. In some experienced center, the procedural success rate can reach roughly 90% [7]. In spite of these improvements, many problems such as acute complications, restenosis and coronary artery aneurysms (CAAs) continue to present a challenge.

CAA is an abnormal dilatation (≥1.5-fold) of part of the coronary artery and often found coincidentally on coronary angiography. There are limited published data focused on CAA formation following PCI supported by drug eluting stent (DES) which is postulated to be associated with hypersensitivity reactions toward the stent [8,9]. As we all know, CTO-PCI has a higher probability of using longer stents and exposing the subintimal structure to the stent, or even stenting subintimally. However, not any retrospective or prospective study was designed to focus on the status and outcomes of CAAs after successful CTO-PCI and DES implantation. Therefore, we designed the current study to investigate the independent predictors and clinical outcomes for CAAs which developed after successful CTO-PCI and DES implantation.

2. Methods

2.1. Study population

We reviewed the catheterization database and medical records at the Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital of Fudan University and identified 697 patients with successful recanalization of CTOs in the native coronary arteries who presented from 2004 to 2010. All patients in the current study received follow-up angiography in the same catheterization center and were divided into CAA group and non-CAA group according to the detection of CAAs. Patients with CTOs were excluded when any of the following was encountered: (1) Procedural failure to open the CTOs; (2) PCI without DES implantation; (3) Previous attempted percutaneous transluminal coronary angioplasty (PTCA) to the target CTO; (4) In-stent restenotic occlusions (Mehran IV pattern restenosis); (5) CAAs observed in any vessel before PCI; (6) Lack of angiographic follow-up in our center; (7) Re-PCI to the target CTO vessel before detection of a CAA in the CAA group; and (8) Duration of angiographic follow-up <6 months in the non-CAA group. A retrospective chart review was performed to collect the clinical variables, history and catheterization information.

The angiographic follow-up duration of the CAA group was defined as the duration from the 1st successful CTO-PCI to the 1st diagnosis of CAA. The angiographic follow-up duration of the non-CAA group was defined as the duration from the 1st successful CTO-PCI to the final recorded angiography unless re-PCI for the target vessel. The long-term clinical follow-up duration of patients in both groups was defined as the time from the 1st successful CTO-PCI to July 31, 2013.

All the CTO-PCI procedures were performed by 10 different operators from our center. All of the operators achieved more than 200 PCI per year. The regulatory board of the Zhongshan Hospital affiliated to Fudan University approved this study. All the patients gave written informed consent before all the procedure.

2.2. Procedures and medications

All the percutaneous revascularizations of CTOs were performed according to the current standard guidelines. All patients were prescribed medicine prior to interventions, with administration of 300 mg aspirin and 300 mg clopidogrel as pretreatment. After operation, all patients were advised to maintain their life-long aspirin therapy, and at least a 12-month clopidogrel prescription.

Intravascular ultrasound (IVUS) was performed using iLAB (Boston Scientific, USA). After the intracoronary administration of nitroglycerin (0.2 mg), the ultrasound catheter (2.5 F Atlantis SR, 40-MHz, Boston Scientific Corporation, USA) was advanced distally to the left anterior descending artery, the left circumflex or the right coronary artery along the 0.014″ guidewire and was pulled back to the aortocoronary ostium using motorized transducer pullback at the speed of 0.5 mm/s. Continuous ultrasound images were obtained and recorded on CDs. The IVUS data were analyzed by two specially experienced cardiologists and one experienced technician.

2.3. Angiographic definitions

CTO is defined as thrombolysis in myocardial infarction (TIMI) grade 0 flow and the duration of coronary occlusion ≥3 months [3]. In the absence of serial angiograms, the duration of coronary occlusion is instead estimated from available clinical information related to the event that caused the occlusion (eg, acute MI or sudden change in angina pattern with ECG changes consistent with the location of the occlusion) [3]. Angiographic success was defined as a restoration of TIMI flow grade 3 in the target vessel after DES implantation and a residual stenosis <10% by visual estimation.

CAA is typically defined as a dilatation in the diameter of a coronary artery segment to more than 1.5-fold the normal size by visual estimation [10], and this CAA was closely related to the underlying DES or its edges, and the localized dilation was absent immediately after the procedure.

The angiographic indices examined were the location of the CTO, CAA, diffuse disease proximal to the occlusion (at least one stenosis of >50% proximal to the occlusion) [11], side branch at the occlusion, vessel tortuosity (the presence of at least one bend of >45° proximal to the occlusion) [11], calcium at the site of the occlusion (radio-opacity present before contrast injection), ostial occlusion (occlusion within 3 mm of the ostium), stump morphology (a blunt or tail-like stump) and grades of bridging collaterals (0 = none; 1 = filling of side branches of the artery to be dilated via collateral channels without visualization of the epicardial segment; 2 = partial filling of the epicardial segment via collateral channels; and 3 = complete filling of the epicardial segment of the artery being dilated via collateral channels) [12]. Angiographic restenosis was defined as a ≥50% diameter stenosis within the target lesion.

All the films were reviewed by two qualified interventional doctors. If there was any ambiguity in the reports or films, the films were reviewed independently by three well-qualified interventional doctors.

2.4. Study endpoints

The major adverse cardiac events (MACEs), including cardiac death, myocardial infarction (MI), and target-vessel revascularization (TVR), were recorded. MI was defined as elevation of the cardiac troponin with at least one value above the 99th percentile of the upper reference limit and with at least one of the following: (1) symptoms of ischemia, (2) new or presumably new significant ST–T changes or new LBBB, (3) development of pathological Q waves in the ECG, (4) imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality, and (5) identification of an intracoronary thrombus by angiography or autopsy [13]. TVR was defined as emergency or elective coronary artery bypass graft or repeat PCI in the target vessel.

2.5. Statistical analysis

The data were expressed as the mean ± SD for the continuous variables, and as frequencies for the categorical variables. The comparison of continuous variables was performed by the independent Student's t-test or the Mann–Whitney U test as appropriate. Statistical analysis of the categorical variables was performed using the Pearson chi-square or Fisher's exact test as appropriate.

The multivariate logistic regression model (the variables in Tables 1, 2 and 3 with $P < 0.1$ were entered into the analysis, except for the

Table 1
Baseline clinical characteristics.

Clinical characteristics	All patients (n = 141)	Patients with CAA (n = 16)	Patients without CAA (n = 125)	P value
Gender, male	119 (84.4)	15 (93.8)	104 (83.2)	0.467
Age, years	60.35 ± 11.28	51.44 ± 11.84	61.49 ± 10.73	0.001
Angina status				
Asymptom	3 (2.1)	0 (0)	3 (2.4)	0.600
Stable	59 (41.8)	5 (31.3)	54 (43.2)	
Unstable	79 (56.0)	11 (68.8)	68 (54.4)	
Smoking	63 (44.7)	6 (37.5)	57 (45.6)	0.539
Hypertension	101 (71.6)	14 (87.5)	87 (69.6)	0.237
Diabetes	37 (26.2)	2 (12.5)	35 (28.0)	0.238
Prior MI	41 (29.1)	5 (31.3)	36 (28.8)	0.779

Data are presented as mean ± SD or n (%). CAA indicates coronary artery aneurysm; MI, myocardial infarction.

angiographic follow-up duration because of its different design) was used to identify the independent predictors of CAAs after successful CTO-PCI and DES implantation. The Cox proportional-hazards model was used to test whether CAA was an independent predictor of clinical outcomes or not. P values were two-tailed, and $P < 0.05$ was considered statistically significant. The data were analyzed with SPSS v.20.0 statistical software (SPSS, version 20.0, Inc., Chicago, IL, USA).

3. Results

Between 2004 and 2010, among 697 patients with successful recanalization of CTOs in the native coronary arteries, a total of 141 patients with 149 CTOs met the inclusion criteria (Fig. 1). In the follow-up angiography, CAAs were observed in 17 (11.4%) lesions of the left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA), respectively (Figs. 2, 3 & 4). Most of the CAAs (13, 76.5%) in the current study were first detected <1 year after the 1st successful procedure. The shortest duration to detect a CAA was 34 days (Fig. 2) which showed no morphological change of the CAA after approximately 7 years (Supplement Fig. 1).

3.1. Baseline characteristics

The baseline clinical characteristics of the patients were represented in Table 1. The mean age of our cohort was 60.4 ± 11.3 years, 84.4% were men, 71.6% had hypertension, 26.2% had diabetes and 29.1% had prior MI. A significant difference of the age (51.4 ± 11.8 versus 61.5 ± 10.7 years, P = 0.001) was shown between the CAA group and non-CAA group. While, there were no significant differences in the other baseline clinical characteristics between the two groups.

3.2. Angiographic and procedural characteristics

Table 2 summarized the angiographic characteristics of all the lesions. The angiographic follow-up duration ranged from 1.1 to 48.5 months in the CAA group and 6.0 to 70.6 months in the non-CAA group. The difference of angiographic follow-up duration between the two groups was significant (P = 0.012) due to the different design. 53.0% occurred with triple-vessel disease, left circumflex arteries (18.1%) were the infrequent CTO location and ostial occlusion accounted for 11.4% (17/149) of the overall lesions. Most of CTO's morphological characteristics which were acknowledged to be

Table 2
Angiographic characteristics.

Angiographic characteristics	All lesions (n = 149)	CAA group (n = 17)	Non-CAA group (n = 132)	P value
Angiographic follow-up duration, months	17.21 ± 14.67	11.04 ± 11.28	18.00 ± 14.90	0.012
IRA	41 (27.5)	5 (29.4)	36 (27.3)	1.000
No. of diseased vessels				
1	20 (13.4)	1 (5.9)	19 (14.4)	0.590
2	50 (33.6)	5 (29.4)	45 (34.1)	
3	79 (53.0)	11 (64.7)	68 (51.5)	
Location of CTO				
LAD	58 (38.9)	5 (29.4)	53 (40.2)	0.152
LCX	27 (18.1)	1 (5.9)	26 (19.7)	
RCA	64 (43.0)	11 (64.7)	53 (40.2)	
Diffuse disease proximal to occlusion	38 (25.5)	3 (17.6)	35 (26.5)	0.562
Side branch at occlusion	33 (22.1)	4 (23.5)	29 (22.0)	1.000
Vessel tortuosity	27 (18.1)	4 (23.5)	23 (17.4)	0.513
Calcification	25 (16.8)	1 (5.9)	24 (18.2)	0.308
Ostial occlusion	17 (11.4)	5 (29.4)	12 (9.1)	0.028
Stump				
No stump	7 (4.7)	1 (5.9)	6 (4.5)	0.745
Blunt stump	54 (36.2)	5 (29.4)	49 (37.1)	
Tail-like stump	88 (59.1)	11 (64.7)	77 (58.3)	
Collateral circulation (grade)				
0	6 (4.0)	0 (0)	6 (4.5)	0.958
1	10 (6.7)	1 (5.9)	9 (6.8)	
2	42 (28.2)	4 (23.5)	38 (28.8)	
3	91 (61.1)	12 (70.6)	79 (59.8)	

Data are presented as mean ± SD or n (%). CAA indicates coronary artery aneurysm; IRA, infarct-related artery; CTO, chronic total occlusion; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 3
Procedural characteristics.

Procedural characteristics	All lesions (n = 149)	CAA group (n = 17)	Non-CAA group (n = 132)	P value
Microcatheter	35 (23.5)	7 (41.2)	28 (21.2)	0.124
Number of guidewire	1.88 ± 0.85	2.12 ± 0.86	1.85 ± 0.85	0.222
Maximal stiffness of guidewire tip				
<3 g	22 (14.8)	1 (5.9)	21 (15.9)	0.340
3–6 g	117 (78.5)	14 (82.4)	103 (78.0)	
6–9 g	3 (2.0)	1 (5.9)	2 (1.5)	
≥9 g	7 (4.7)	1 (5.9)	6 (4.5)	
Guidewire technique				
Parallel wire technique	29 (19.5)	9 (52.9)	20 (15.2)	0.001
Seesaw technique	5 (3.4)	1 (5.9)	4 (3.0)	0.459
Side branch technique	2 (1.3)	0 (0)	2 (1.5)	1.000
Retrograde wire technique	4 (2.7)	0 (0)	4 (3.0)	1.000
Predilation				
Size of initial predilation balloon, mm	1.78 ± 0.45	1.66 ± 0.36	1.79 ± 0.46	0.416
Stepwise predilation (from small to large balloon)	90 (60.4)	13 (76.5)	77 (58.3)	0.150
IVUS	7 (4.7)	2 (11.8)	5 (3.8)	0.183
DES				
Total length, mm	54.37 ± 23.52	69.18 ± 17.92	52.46 ± 23.53	0.005
Postdilation with non-compliant balloon	24 (16.1)	4 (23.5)	20 (15.2)	0.480
Drug of DES				
Paclitaxel	22 (14.8)	1 (5.9)	21 (15.9)	
Sirolimus	119 (79.9)	15 (88.2)	104 (78.8)	0.590
Zotarolimus	8 (5.4)	1 (5.9)	7 (5.3)	
Polymer of DES				
Durable polymer	129 (86.6)	14 (82.4)	115 (87.1)	0.598
Biodegradable polymer	17 (11.4)	3 (17.6)	14 (10.6)	
Mixed usage	3 (2.0)	0 (0)	3 (2.3)	

Data are presented as mean ± SD or n (%). CAA indicates coronary artery aneurysm; PCI, percutaneous coronary intervention; IVUS, intravascular ultrasound; DES, drug-eluting stent.

associated with procedural success showed no significant difference between the two groups. In particular, ostial occlusion (29.4% versus 9.1%, P = 0.028) was the only factor associated with CAAs after successful CTO-PCI and DES implantation.

3.3. Procedural characteristics

The procedural characteristics including devices and techniques were shown in Table 3. The average number of the used guidewire was 1.9 ± 0.9 and stiffness of the guidewire tip focused from 3 to 6 g. The single-wire technique was the predominant strategy used in 114 cases (76.5%) followed by the parallel wire technique in 29 cases (19.5%). The seesaw technique (5, 3.4%), side branch technique (2, 1.3%) and retrograde wire technique (4, 2.7%) were rarely used in the lesions including in the current study. The average DES length was 54.4 ± 23.5 mm. The most frequently used stents were durable polymer stents (129, 86.6%) and sirolimus eluting stents (SES) (119, 79.9%). The assumed influencing factors including number of guidewire, stiffness of guidewire tip, predilation, drug and polymer of DES showed no significant differences between the two groups. However, the use of the parallel wire

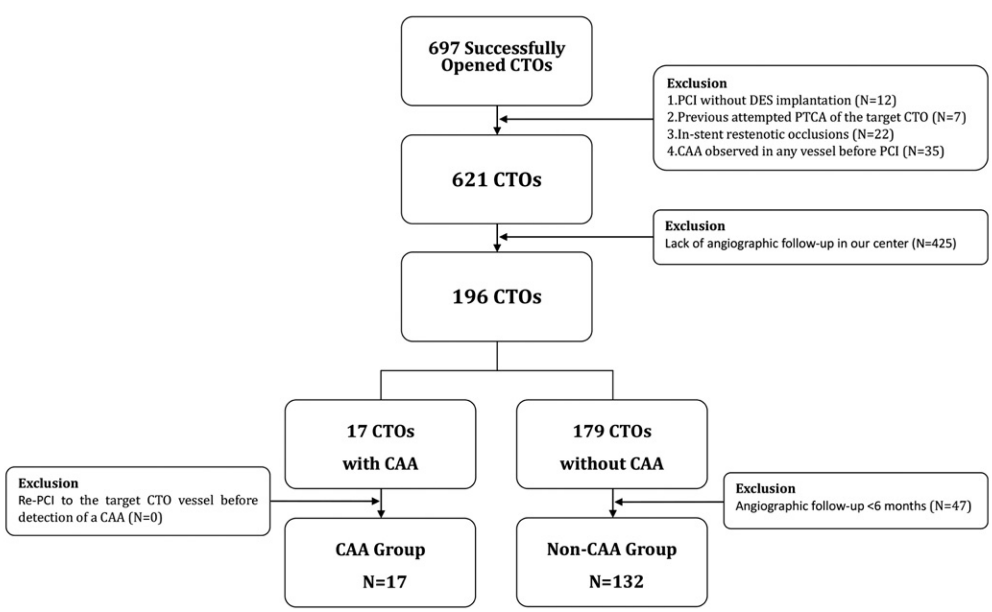

Fig. 1. The schema of patients enrolled. This figure depicts how patients with successfully opened CTOs during the study period (2004–2010) were dispatched and selected. CTO indicates chronic total occlusion; DES, drug-eluting stent; PCI, percutaneous coronary intervention; CAA, coronary artery aneurysm.

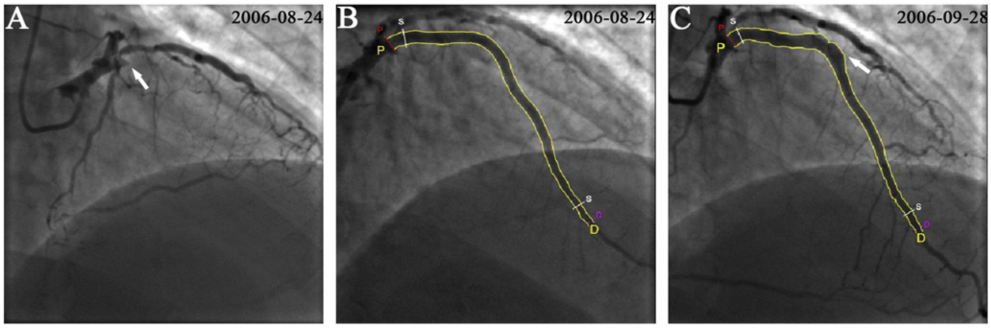

Fig. 2. Development of a CAA in left anterior descending artery after successful CTO-PCI and DES implantation. Panel A shows the initial lesion at August 24, 2006 and percutaneous coronary intervention was performed. After stent implantation with paclitaxel-eluting stents 3.0 × 32 mm, 2.75 × 32 mm and 2.5 × 16 mm (B), a huge CAA was apparent on the follow-up angiography at 34 days (C). CAA indicates coronary artery aneurysm; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; DES, drug-eluting stent.

technique (52.9% versus 15.2%, $P = 0.001$) and DES length (69.2 ± 17.9 versus 52.5 ± 23.5 mm, $P = 0.005$) were associated with more CAAs after successful CTO-PCI and DES implantation.

3.4. Multiple logistic regression analysis

The multiple logistic regression analysis (Table 4) revealed that age (OR: 0.925, CI 0.873–0.980, $P = 0.008$), ostial occlusion (OR: 6.715, CI 1.473–30.610, $P = 0.014$), the parallel wire technique (OR: 6.167, CI 1.709–22.259, $P = 0.005$) and DES length (OR: 1.030, CI 1.002–1.058, $P = 0.036$) were the independent predictors of CAAs after successful CTO-PCI and DES implantation.

3.5. Outcomes

During a mean follow-up period of 3.9 ± 1.6 years which included at least once angiographic follow-up in all patients, 127 patients (90.1%) completed follow-up. The MACEs at 5-year follow-up of the CAA group and non-CAA group were shown in Table 5. Aspirin was prescribed after discharge for 93.8% (15/16) of patients with CAAs and 96.8% (121/125) of patients without CAAs ($P = 0.457$). Clopidogrel (at least 12-months) was definitely prescribed after discharge to all the patients included in the current study. The main reason for discontinuing aspirin was gastrointestinal side-effect and bleeding. During the 5-year follow-up, MACEs were observed in 3 patients (18.8%) in the CAA group and 25 patients (20.0%) in the non-CAA group. There were no cardiac deaths and MI in the CAA group. Four cardiac deaths (3.2%) due to 3 acute MI and 1 severe heart failure were observed in the non-CAA group. TVR was observed in 3 patients (18.8%) in the CAA group and 22 patients (17.6%) in the non-CAA group. Overall, there were no statistical differences of MACEs between the two groups under the dual antiplatelet therapy (adjusted hazard ratio 0.670; 95% CI 0.160–2.808; $P = 0.584$).

4. Discussion

CAAs were observed in 0.15–4.9% of the patients undergoing coronary angiography [14]. Compared with other etiologies, the formation of CAAs after PCI is relatively rare. The reported incidence of CAAs is 0.3% to 6.0% for PTCA [15–18], and 0.2% to 10.5% for DES implantation [8,19–23]. Compared with non-CTOs, our findings showed a slightly high incidence (11.4%) of CAA detection after successful CTO-PCI and DES implantation.

4.1. Duration of CAA detection after PCI

In previous studies, duration of CAA detection after PCI is quite variable [24–27]. In one recent study by Kim which included 28–36 months of angiographic follow-up [23], most of the CAAs after DES implantation were detected > 1 year after the initial procedure. However, 76.5% (13/17) of the CAAs in the current study were firstly detected < 1 year after the 1st successful PCI. And the shortest duration to detect a CAA was only within 34 days. This difference of incidence and detection time resulted from many factors such as particular institution, operator experience and patient characteristics. But we believed that the most important factor was the design of the multiple angiographic follow-up which would increase the detection of late occurrence of CAA. Thus, the published data came to the conclusion that the duration of CAA detection after PCI was replete with uncertainty, largely because they were not formed by a single factor, but the result of multiple ones.

4.2. Predictors of CAAs after successful CTO-PCI and DES implantation

The development of CAAs after PCI was reported to be a consequence of non-procedural factors and procedural factors. Among the non-procedural factors, age (OR: 0.925, CI 0.873–0.980, $P = 0.008$) and ostial occlusion (OR: 6.715, CI 1.473–30.610, $P = 0.014$) were found to be the

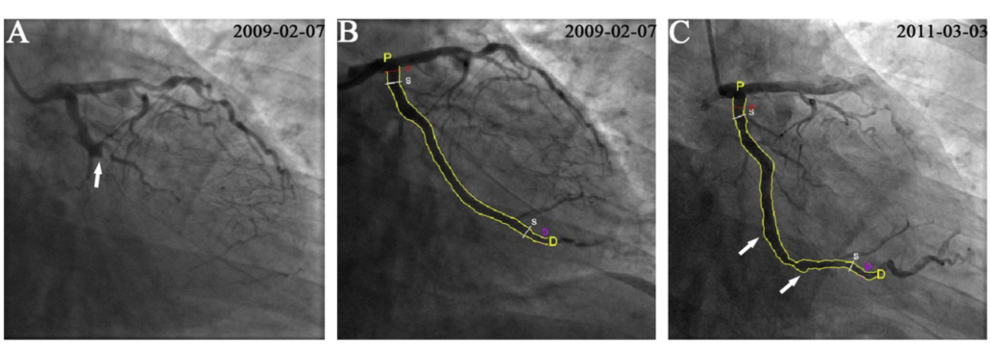

Fig. 3. Development of CAAs in the left circumflex artery after successful CTO-PCI and DES implantation. This figure depicts the initial lesion at February 07, 2009 and percutaneous coronary intervention was performed (A). After stent implantation with sirolimus-eluting stents 3.0 × 36 mm and 2.5 × 36 mm (B), two focal CAAs (white arrow) were apparent on the follow-up angiography at March 03, 2011 (C). CAA indicates coronary artery aneurysm; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; DES, drug-eluting stent.

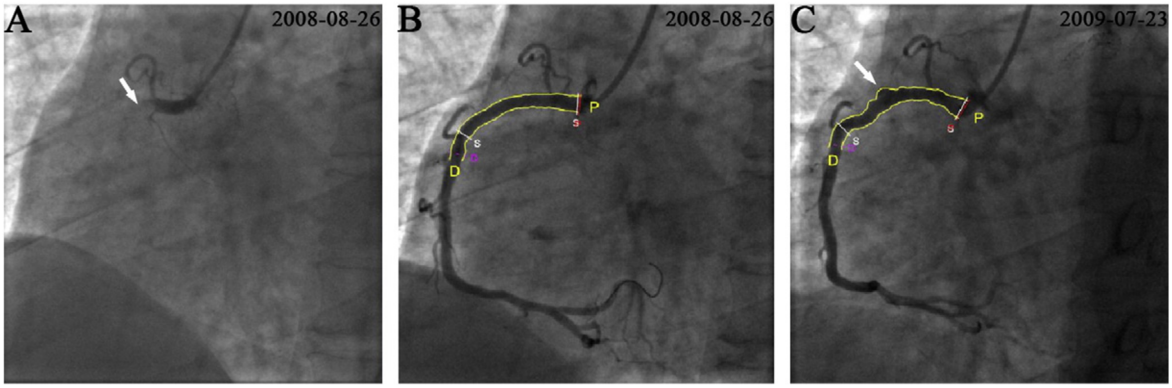

Fig. 4. Development of a CAA in the right coronary artery after successful CTO-PCI and DES implantation. This figure depicts the initial lesion at August 26, 2008 and percutaneous coronary intervention was performed (A). After stent implantation with sirolimus-eluting stents 3.5 × 33 mm (B), a CAA (white arrow) was apparent on the follow-up angiography at July 23, 2009 (C). CAA indicates coronary artery aneurysm; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; DES, drug-eluting stent.

independent predictors of CAAs after successful CTO-PCI and DES implantation in the current study. The exact mechanism of susceptibility related to age has not yet been clarified. However, the relevance of the relationship between young age and coronary positive remodeling has been reported in some previous studies [28,29]. Our findings shared the similar mechanism; subsequently, larger clinical trials are warranted to confirm this finding. Ostial lesions have been recognized as a challenge for CTO-PCI because of difficulties in the placement of a guiding catheter and poor back-up support [30–33]. To some extent, these difficulties can indirectly increase the risks for vessel injury which may contribute to the CAA formation. On the other hand, among all the procedural factors, the parallel wire technique (OR: 6.167, CI 1.709–22.259, $P = 0.005$) and DES length (OR: 1.030, CI 1.002–1.058, $P = 0.036$) were found to be the independent risk factors of CAAs after successful CTO-PCI and DES implantation in the current study. During our CTO-PCI, the single-wire technique was the predominant strategy used in 114 cases (76.5%) followed by the parallel wire technique in 29 cases (19.5%). Generally, when the single wire technique had failed to run through the real lumen, the parallel wire technique logically became the primary basic technique for CTO-PCI. Nevertheless, in spite of its contribution to the success of CTO-PCI, the parallel wire technique seemed to increase the risks of CAA formation in the current study. The potential cause was that the 1st wire had already entered the subintima and created a false lumen before the parallel wire technique was performed. Hereby, even though the 2nd wire increased the success rate of CTO-PCI, the parallel wire technique could not remedy and improve the preexisting damage to the artery wall. It was consistent with the compelling evidence provided by our study. Furthermore, DES length was one of the risk factors for CAAs after DES implantation reported generally [23]. Our study reached the same conclusion.

4.3. Mechanism of CAAs after successful CTO-PCI and DES implantation

A new classification had been suggested to identify the cause of CAAs after PCI, including arterial injury, the chronic arterial response to the DES and infection [9]. Among them, arterial injury related to the procedure was postulated to be a more likely contributor to the rapid development of an aneurysm after PCI than the chronic arterial response secondary to a hyper-sensitivity reaction to the stent polymers and drugs [8,9]. During the procedure, balloon over inflation or other iatrogenic injury had already been reported to be the independent risk factor for CAAs after DES implantation in previous observational studies [15–17]. In view of the evidence provided by IVUS, the parallel wire technique was obviously associated with arterial wall injury. The mechanism lied in that the subintimal passage of the guidewire, creation of a false lumen, and stenting within the false lumen might result in injury to the adventitial layer during CTO-PCI. Therefore, it provided evidence to us that arterial injury was the very important mechanism responsible for CAAs after successful CTO-PCI. Otherwise, in terms of chronic arterial response which was proved by the finding of an eosinophilic infiltrate in the few cases of such poststent coronary artery aneurysms examined histologically [34,35], long DES of CTO-PCI would aggravate this situation. Overall, the formation of CAAs in this procedure was a combined event including clinic characteristics, angiographic morphology, various techniques, and DES selection, which was beyond doubt.

4.4. Outcomes of CAAs after successful CTO-PCI and DES implantation

Up to now, the clinical implications of CAAs have not been definitely determined. Hereby, it is very important and necessary for assessing and detecting potentially harmful complications of CAAs after successful CTO-PCI and DES implantation. In some studies, CAAs related to DES had been suggested predispose to stent thrombosis [23,36]. However, no statistical difference of MACEs between the CAA group and non-CAA group was shown in the current study. Therefore, in this study, CAAs after successful CTO-PCI and DES implantation were not frequently associated with adverse clinical events under the current dual antiplatelet regimen. Based on these data, it could be conjectured that MACEs might originate mainly from natural progression of coronary artery diseases, not just only from CAAs themselves. For better understanding this complication, further large clinical trials and follow-up studies are needed.

In conclusion, our work represents the first study to indicate the independent predictors of CAAs after successful CTO-PCI and DES implantation, which included age, ostial occlusion, the parallel wire technique and DES length. Furthermore, we also demonstrated for the first time that CAAs after the index procedure would not increase MACEs under dual antiplatelet therapy at 5-year follow-up, compared with the non-CAA group. These results could improve our understanding of therapeutic intervention in cardiovascular diseases.

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Table 4
Multivariate logistic regression analysis for independent predictors of CAAs after CTO-PCI and DES implantation.

	OR	95%CI	P value
Age	0.925	0.873–0.980	0.008
Ostial occlusion	6.715	1.473–30.610	0.014
Parallel wire technique	6.167	1.709–22.259	0.005
Length of DES	1.030	1.002–1.058	0.036

CAA indicates coronary artery aneurysm; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; DES, drug-eluting stent.

Table 5
Clinical outcomes at 5-year follow-up.

	Patients with CAA (n = 16)	Patients without CAA (n = 125)	Unadjusted HR (95% CI)	P value	Adjusted HR[a] (95% CI)	P value
Cardiac death	0 (0)	4 (3.2)		1.000		1.000
Myocardial infarction	0 (0)	3 (2.4)		1.000		1.000
Target vessel revascularization	3 (18.8)	22 (17.6)	0.979 (0.293–3.272)	0.973	0.804 (0.187–3.467)	0.770
MACEs	3 (18.8)	25 (20.0)	0.866 (0.261–2.868)	0.813	0.670 (0.160–2.808)	0.584

Data are presented as mean ± SD or n (%). CAA indicates coronary artery aneurysm; MACE, major adverse cardiac event, CI, confidence interval; HR, hazard ratio.
[a] Adjusted covariates included male, age, history of smoking, diabetes, prior myocardial infarction, triple-vessel disease, ostial occlusion, parallel wire technique, length of drug-eluting stent.

Limitation

This study had two limitations. First, this study was not a prospective randomized trial from multiple centers. The occurrence of MACE events might be confounded with some factors such as different reasons for repeat coronary angiogram. Second, the precise duration of the occlusion was not angiographically documented, a limitation applicable to all observational studies of CTOs.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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